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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,323	07/09/2003	Laurence A. Cole	MBHB 03-411-A	1369

7590 05/29/2008

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/616,323	COLE, LAURENCE A.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-16,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-16,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed July 16, 2007 in response to the Office Action of January 11, 2007 is acknowledged and has been entered. Previously pending claims 3, 4 have been cancelled, claims 1 and 12 have been amended and new claims 46 and 47 have been added.

2. Claims 1, 2, 5-16, 46, and 47 are currently being examined.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4 Claims 1, 5-8, 10 and 11 remain rejected under 35 USC 112 2nd paragraph for the reasons previously set forth in the Office Action of January 11, 2007, section 10, pages 5.

Applicants have not made arguments or amendments to overcome this rejection, so for the reasons previously set forth, the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5 Claims 1, 2, and 5-16 remain rejected and new claims, 46, and 47 are rejected under 35 USC 112 1st paragraph for the reasons previously set forth in the Office Action of January 11, 2007, section 12, pages 6-8.

Applicants argue the claimed invention is enabled. Applicants argue that the invention as claimed relates to a method for measuring the total amount of intact hCG and ITA or the total amount of intact hCG and ITA plus the free beta form of hCG in a biological sample from a

patient at risk for invasive trophoblastic disease or quiescent gestational trophoblastic disease as claimed and determining the amount of total intact hCG plus ITA or total hCG plus beta core plus ITA with the amount of ITA measured in the sample such that a diagnosis of invasive trophoblastic disease or quiescent gestational trophoblastic disease may be made.

Applicants argue that the measurement of the amount of intact hCG, ITA and beta core hCG as defined in the specification in a urine, serum or plasma sample is well known in the art. The approach to measuring this amount may be through an immunoassay, or other commercially available hCG tests. Indeed many commercial assays measure same. This is discussed in significant detail in the specification inter alia, at page 7, fourth full paragraph of the specification, as well as on pages 8-10. Approaches for measuring hCG in biological samples have been known for years and are well documented and routine in the art. The measurement of ITA as defined in the specification (containing both N-glycosyl linkages and O-glycosyl linkages as indicated in the specification) is also well known in the art. Analysis can be performed by any number of techniques as described in the present application at pages 8-10 and in particular, in an immunoassay using the B 152 antibody which is specific for ITA (and the O-glycosyl linkages of ITA as explained in the Valmu, et al. paper). Other methods are readily adapted from prior art teachings. Thus the present invention relates to the measure of ITA as opposed to the N-glycosylated variant measured by Kobata and provides a well-known method available in the art including a specific monoclonal antibody B152 which is specific for ITA.

Applicants argue that that the amount of intact hCG, ITA and optionally, beta hCG as claimed may be measured using any number of methods which are available in the art and are well described in the literature. In addition, as noted, commercial immunoassays may also be

utilized to measure hCG and may be preferably used. These may be used directly or adapted with minor variation in order to obtain an amount of hCG in a sample. Antibodies are readily available commercially which may measure intact hCG and ITA, and optionally, beta hCG as defined in the specification. Regarding the measurement of ITA, the preferred method for measuring ITA in a sample is through the use of monoclonal B 152, which is readily available. Thus, all of the components for practicing the invention are available and well known in the art, all of the steps are well known and practicing the method which simply relies on well known steps already known in the art using components which are readily available in the art evidences that the claimed method is clearly enabled.

Applicant's argument has been considered, but has not been found persuasive. Although assays to measure glycosylated hCG are well known in the art the specialized "in house" assays described in the specification to measure hCG/ITA are not described and are not known in the art. Additionally Applicant has previously argued that the measurement of N-linked ITA, which is encompassed by the claims, is much less reliable than measuring O-linked ITA and currently argue that methods such as that of Kobata to measure N-linked ITA have relatively low accuracy compared to the method of present application, see 1st para. of page 8 of the remarks of July 16, 2007. Given that the specification provides neither information nor guidance on how to make and use the specialized "in house" assays for measuring hCG/ITA and nor guidance on how to measure ITA as claimed when the measurement of N-linked ITA is much less reliable than measuring O-linked ITA or of relatively low accuracy, undue experimentation would be required to practice the method as claimed.

It is also noted that the B152 monoclonal antibody does not distinguish between N-linked and O-linked hyperglycosylated hCG, see Example 3 of US Pat. 6,429,018, which was incorporated by reference in the specification. Thus, if the measurement of N-linked hCG is less reliable and has low accuracy, the use of the B152 antibody would not obviate this problem.

Applicant's arguments have not been found persuasive and the rejection is maintained.

6. Claims 12 remains rejected and new claim 47 is rejected under 35 USC 112 1st paragraph for the reasons previously set forth in the Office Action of January 11, 2007, section 14, pages 10-13.

Applicant argues that Applicant has amended claim 12 to reflect an inventive method which is enabled. In particular, the method is directed to a method of diagnosing quiescent gestational trophoblastic disease in a patient at risk for that disease. Applicant argues that gestational trophoblastic disease is described in the specification on pages 6, second full paragraph, and is otherwise described on page 10 of the specification. Applicant argues that the method of claim 12, which provides for steps related to determining levels of hCG and ITA and optionally beta hCG in a biological sample in a patient at risk for quiescent gestational trophoblastic disease is clearly enabled. Applicant argues that each of the delineated steps is well known, each of the components which may be used to measure individual values as described in the claim are readily available and performing the steps as set forth in amended claim 12 is routine. Claim 12 is enabled.

Applicant's argument has been considered, but has not been found persuasive because without any prior diagnosis of gestational trophoblastic disease it cannot predictably be determined that a patient is at risk for quiescent gestation trophoblastic disease because of the

low levels of hCG and ITA that are found in any healthy, nonpregnant individual as previously set forth.

Applicant's arguments have not been found persuasive and the rejection is maintained.

7. Claims 1, 2, and 6-16 remain rejected and new claim 47 is rejected under 35 USC 112 1st paragraph for the reasons previously set forth in the Office Action of January 11, 2007, section 15, pages 13-17.

Applicant has amended the claims to determining the amount of hCG in the sample wherein the amount of hCG comprises the total amount of intact hCG and ITA in the sample or comprises the total amount of intact hCG plus the amount of free β subunit of hCG and ITA in the sample, apparently to overcome this rejection, but no specific arguments to this rejection were presented.

Applicant's amendment has been considered, but has not been found persuasive because the comprising language in the claims still encompasses measuring other forms of hCG that are ITA, as contemplated in the specification as previously set forth.

Applicant's amendment has not been found persuasive and the rejection is maintained.

8. Claims 1, 2, and 6-16 remain rejected and new claim 47 is rejected under 35 USC 112 1st paragraph for the reasons previously set forth in the Office Action of January 11, 2007, section 16, pages 18-21.

Applicant argues that the present claims now adequately directed to measuring the amount hCG (intact hCG plus ITA alone or in combination with beta hCG) which is measured to provide the presently claimed method. That is now adequately described in the specification and set forth in the claims. A review of the claimed subject matter and the specification clearly

evidences that the present invention is now in compliance with the requirements of 35 U.S.C. § 112, first paragraph as related to the written description requirement. The present invention must be seen to be in compliance with the requirements of 35 U.S.C. § 112, first paragraph.

Applicant's argument has been considered, but has not been found persuasive because the comprising language in the claims still encompasses measuring other forms of hCG for detecting the presence of invasive trophoblast cells or diagnosing quiescent gestational trophopblasitc disease as contemplated in the specification and thus, as previously set forth the specification the claims are not adequately supported by a written description.

Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection/Objection

Claim Objections

9. Claim 12 is objected to because of the following informalities: The word "determining" in step b. is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2, 6-8, 10 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kobata (Biochimie, 1988, 70: 1575-1585, previously cited) as evidenced by Cole and Butler (J. Reproductive Medicine, June 2002, 47: 433-444, IDS item).

The claims are drawn to:

1. A method of detecting the presence or absence of invasive trophoblast cells in a patient at risk for invasive trophoblast disease comprising the steps of: a. obtaining a urine, saliva, serum or plasma sample from a said patient;

b. determining the amount of hCG in the sample wherein the amount of hCG comprises the total amount of intact hCG and ITA in the sample or comprises the total amount of intact hCG plus the amount of free β subunit of hCG and ITA in the sample;

c. determining the total amount of ITA in the sample;

d. determining the percentage of the amount of hCG that is ITA, and

e. determining that invasive trophoblast cells are present in the patient if the percentage is 30% or greater.

2. The method of claim 1, wherein the amount of hCG is comprises the total amount of intact hCG and ITA plus the amount of free β subunit of hCG in the sample.

6. The method of claim 1, wherein the patient is a woman previously diagnosed as having a gestational trophoblastic disease.

7. The method of claim 6, wherein the gestational trophoblastic disease is hydatidiform mole.

8. The method of claim 6, wherein the gestational trophoblastic disease is choriocarcinoma.

10. The method of claim 1, wherein the biological sample is urine, plasma or serum.

11. The method of claim 10 wherein the biological sample is urine.

It is noted that the specification teaches that the term "intact" or "regular" hCG is used herein to refer to hCG that is composed of two dissimilar subunits, α (92 amino acids and two N-

linked oligosaccharides) and β (145 amino acids and two N-linked and four O-linked oligosaccharides), that are joined noncovalently, see p. 4, lines 21-24.

Given that the specification does not define a patient at risk for invasive trophoblast disease in a limiting manner and that a gestational trophoblastic disease is characterized by abnormal cellular growth of the tissues formed as a result of conception, leading to the development of tumors within the uterus, see p. 1, lines 13-15 it assumed for examination purposes that any pregnant woman or person diagnosed with a gestational trophoblastic disease is at risk for invasive trophoblast disease.

Kobata teaches, as previously set forth on page 4 of the Office Action of May 30, 2006, a method obtaining a biological sample wherein the biological sample is urine from a patient previously diagnosed with a trophoblastic disease or a pregnant woman (pg. 1582, right column and Figure 9). Additionally, Kobata teaches measuring total hCG and the percentage of hCG that is hyperglycosylated hCG (page 1582, right column and Figure 9), which is ITA. Finally, Kobata teaches the amount hCG that is ITA is greater than 30% in invasive mole and choriocarcinoma patients and less than 30% in the samples from hydatidiform mole patients (Figure 9). Kobata teaches that hCG is composed of 2 subunits, a and b, that contain aspargine linked sugar chains, see p. 1579, *Structures of the sugar chains of hCG.*

Cole and Butler teach that, in addition to regular (intact) hCG, free hCG β-subunits are present in serum and urine samples of patients with trophoblastic diseases and non-trophoblastic neoplasms, see p. 434, 1st col.

Given that Cole and Butler teach that intact hCG and free β-subunits are present in urine of patients with trophoblastic diseases, the method of the prior art comprises the same method as

claimed in the instant invention, that is a method comprising the step of *determining the amount of hCG in the sample*, thus the claimed method is anticipated because the method will inherently be a method comprising the step of *determining the amount of hCG in the sample wherein the amount of hCG comprises the total amount of intact hCG and ITA in the sample or comprises the total amount of intact hCG plus the amount of free β subunit of hCG and ITA in the sample*. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the method determines the *total amount of intact hCG plus the amount of free β subunit of hCG*, the claimed method appears to be the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA)

Applicant argues that it is the Examiner's continued contention that Kobata teaches a method of measuring ITA in a urine sample and on the basis of the percentage of ITA compared to the total amount of hCG in the sample, detecting invasive trophoblast cells if the percentage of ITA in the sample is greater than 30% of the total amount hCG. Applicant argues that the variant of hCG which is measured by Kobata is *not* the same as the variant measured by present invention.

Applicants argue that Applicant's method is clearly patentable and *not* anticipated by the method of Kobata simply because Kobata teaches measuring a variant of hCG which is not ITA,

as that term has been defined in the specification. In particular, Kobata is directed to measuring an N-linked glycosylated variant of hCG, not a glycosylated version of hCG containing O-linked glycosyl as in the present invention (note that ITA, unlike the Kobata glycosylated hCG, contains both N-linked and O-linked glycosyl groups, whereas Kobata contains exclusively N-linked groups). This is explained in great detail in the previously submitted Valmu, et al. article. In as much as there are a number of glycosylated variants, it is the type of variant which will determine the accuracy of the assay and whether or not invasive trophoblast cells exist in a patient. In the case of Kobata, Kobata is measuring N-linked glycosylated versions of hCG, not ITA of the present invention, which is a hyperglycosylated variant of hCG which contains both N-linked and O-linked glycosyl groups.

Applicant's arguments have been considered, but have not been found persuasive because neither the definition of ITA nor the claims are limited to the O-linked glycosylated variant hCG. Thus, applicant is arguing limitations not recited in the claims.

Applicants argue that the definition of ITA, the O-linked glycosylated variant which is measured in the present invention, is set forth in the specification at page 5, in the second full paragraph. This is the variant which Applicant has focused on and to which the present invention is directed to measuring. This is not what Kobata is measuring. The two types of hyperglycosylated variants of hCG, i.e., those of Kobata and those of the present invention, are quite distinguishable. This is clearly presented in Valmu, et al. at page 1213 and in particular, in the first full paragraph bridging the first and second columns. That disclosure clearly evidences that Kobata is measuring an N-glycosylated variant of hCG, not the variant ITA of the present invention. Moreover, Valmu, et al. points out that the Kobata N-glycal hCG variant could not be

detected by the mass-matching approach because the structures carry the same mass as ordinary biantennary N- glycals. This structural feature of the hCG variant measured by Kobata makes its measurement difficult given its similarity in structure to related variants. This would also explain the relatively low accuracy of the Kobata method compared to the method of present application. Applicant argues that it is clear from Valmu, et al. that the Kobata measured hCG variants are clearly distinguishable from ITA, the variant measured in the present invention. See Valmu, et al. also at page 1216, first full paragraph in the left column. Given the fact that the present invention and Kobata measure two distinguishable types of glycosylated hCG as evidenced by the teachings of Valmu, et ah, the method of Kobata does not anticipate the present invention.

Applicant's arguments have been considered, but have not been found persuasive because a review of the second full paragraph on page 5 revealed that the specification teaches that: "ITA" is an abbreviation for invasive trophoblast antigen, also known as hyperglycosylated hCG. ITA is, therefore, a variant of regular hCG, comprising additional side chains of sugars on the N-linked and O-linked sugar chains compared with regular hCG. These additional sugar side chains comprise N-acetylglucosamine, galactose and sialic acid and make the molecule considerably larger in size. Thus the claims as currently set forth are not limited to the N-linked or O-linked form of ITA and applicant is arguing limitations not found in the claim. In addition, as set forth above, applicant is arguing limitations not recited in the claims as currently constituted.

Furthermore, it is noted that Valmu et al. at page 1213 simply teach a limitation of their own method and not a refutation of the findings or accuracy of Kobata and Valmu et al. teach at page 1216 that changes N-linked, Asn-13, were observed in the glycan structure of hCG and not

simply changes in O-linked glycosylation. Thus Valmu et al. do not show that hyperglycosylated hCG measured by Kobata is distinct from the ITA of the instantly claimed method.

Applicants argue that in contrast to the present method, Kobata *only* deals with and measures N-linked glycosylated hCG, not the O-linked glycosylated hCG which is measured in the present invention. Thus, the present invention clearly distinguishes over Kobata in measuring a different hCG variant (known as HhCG or ITA) than Kobata. Thus, because Kobata is not directed to the same or identical method as the present invention (because of the clearly distinguishable variants which are measured in the disclosure of Kobata vs. the present method), Kobata does not and *cannot* anticipate the present invention. Applicants argue that Valmu, et al. clearly shows that the O-linked glycosylated hCG variant ITA, which is measured in the present method, is distinguishable from the N-linked glycosylated hCG which is measured by Kobata, as discussed above. Not only does the enclosed paper show the distinction between the N-linked and O-linked glycosylated variants of hCG, but also points to the superiority of measuring ITA- which is the only significant and consistent change in choriocarcinoma. Thus, Kobata, clearly is directed to measuring a different hCG variant and the disclosed method clearly does not anticipate the present invention.

Applicant's arguments have been considered, but have not been found persuasive because the claims are not limited to the O-linked glycosylated variant hCG. Thus, applicant is arguing limitations not recited in the claims. Furthermore Valmu et al, as set forth above, does not distinguish the glycosylated hCG of Kobata from the ITA of the instant invention.

Applicant argues that the Examiner continues to argue that Applicant, in order to distinguish Kobata, recites limitations which are not in the claims. Applicant argues that the fact

that Applicant recites ITA in the claims is a distinguishable limitation in the claims because ITA, which contains O-linked glycosyl groups as defined in the specification and as described in Valmu, et al., is distinguishable from the hCG variant measured in Kobata, which is directed to a different form of glycosylated hCG containing N-linked glycosyl groups. These hCG variants are clearly not the same and are clearly distinguishable. Given the fact that ITA and the hCG variant of Kobata are distinguishable, as evidenced by the clear description in Valmu, et al., the present claims are not anticipated by the art of record and the distinguishable limitation *is found* in the presently pending claims.

Applicant's arguments have been considered, but have not been found persuasive because the claims are not limited to the O-linked glycosylated variant hCG. Thus, applicant is arguing limitations not recited in the claims. Furthermore Valmu et al, as set forth above, does not distinguish the glycosylated hCG of Kobata from the ITA of the instant invention. Applicant can obviate the instant rejection by clearly directing the claims to the O-linked form of ITA that functions as claimed, given that support for such amendment can found in the specification as originally filed.

Applicant's arguments have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 5 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobata (Biochimie, 1988, 70: 1575-1585, previously cited) as evidenced by Cole and Butler (J. Reproductive Medicine, June 2002, 47: 433-444, IDS item) as applied to claims 1, 2, 6-8, 10 and 11 above, and further in view of Cole et al. (Clin. Chem, 1997, December 2001 47: 308-315, IDS).

The claims are drawn to:

5. The method of claim 1, wherein the amount of hCG is total intact hCG plus ITA in tile sample.

46. The method of claim 1, wherein the amount of hCG consists of intact hCG plus ITA.

Kobata teach as set forth above.

Kobata does not specifically teach the method of claim 1, wherein the amount of hCG is total intact hCG plus ITA in tile sample or wherein the amount of hCG consists of intact hCG plus ITA.

Cole et al. teach that hCG is composed of two a and b subunits joined noncovalently, see p. 308, 2nd col. Cole et al. teach that precise hCG determination are crucial in patients with trophoblastic disease to assess the mass of tumor, the successful treatment of malignancy, or recurrence or persistence of disease. Cole et al. teach that in trophoblastic disease hyperglycosylated hCG is one of the principal sources of immunoreactivity in serum, see p. 309 1st col. Cole et al. teach several immunoassays, including the DPC immunilite assay and the Chiron ACS:180 hCGβ tests, that can individually measure the different forms of hCG, including intact hCG, see Abstract and Table 1. Cole et al. teach that textbooks on obstetrics and

gynecology emphasized the essentiality of hCG testing patients with trophoblastic disease, see p.313, 1st col.

It is noted that the specification teaches that the term "intact" or "regular" hCG is used herein to refer to hCG that is composed of two dissimilar subunits, α (92 amino acids and two N-linked oligosaccharides) and β (145 amino acids and two N-linked and four O-linked oligosaccharides), that are joined noncovalently, see p. 4, lines 21-24.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention and one of skill in the art would have been motivate to measure total intact hCG plus ITA given Kobata teaches an increase in hCG that is ITA of greater than 30% in invasive mole and choriocarcinoma and Cole et al. teach that precise hCG determination are crucial in patients with trophoblastic disease and also teach several standard assays that can measure the various forms of hCG, including regular, intact hCG and hyperglycosylated hCG. Thus, one of ordinary skill in the art would have been motivated with a reasonable expectation of success to measure intact hCG plus ITA given the importance of these measurements in trophoblastic disease.

Claim Rejections - 35 USC § 112

12. Claims 12 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear from the claims or the teachings of the specification how a patient can be at risk for a quiescent disease. Are all healthy individuals at risk for the quiescent disease or just a subpopulation of individuals? Thus the metes and bounds of the claims cannot be determined.

13. Claims 1, 2, 5-16, 46, and 47are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitations of *a patient at risk for invasive trophoblast disease* claimed in Claim 1 and *a patient at risk for quiescent gestational trophoblastic disease* claimed in Claim 12 has no clear support in the specification and the claims as originally filed. A review of the specification did not discloses support for *a patient at risk for invasive trophoblast disease or a patient at risk for quiescent gestational trophoblastic disease,* although support was found for *a patient at risk for* ***gestational*** *trophoblast disease*, see p. 6, lines 23-28. Thus, the subject matter claimed in claims 1, 2, 5-16, 46, and 47 broadens the scope of the invention as originally disclosed in the specification.

14. All other objections and rejections recited in the Office Action of January 11, 2007 are withdrawn.

15. No claims allowed.

16. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application

which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

15. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0890. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

PJR